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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/667,738	09/22/2003	EmadEldin M. Hassan	Hassan2001A	1894

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/667,738	HASSAN, EMADELDIN M.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-45* is/are pending in the application.

4a) Of the above claim(s) *29-32 and 34-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-28 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group IV, claims 26-28 and 33 filed March 24, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 29-32 and 34-45 are non-elected inventions and withdrawn from consideration, thus, claims 26-28 and 33 are examined.

Claim Objections

2. Claims 26-28 are objected to because the claim contains recitation of non-elected water insoluble materials.

Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 26-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U. S. Patent 6,623,761. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 26-28 in the instant application disclose a method for making nanopadicles of a

substantially water insoluble material such as an antimicrobial agent, an antibacterial agent, an antifungal agent, an antiviral agent, an anti-HIV drug, an immunosuppressant, an anticancer agent and an antidiabetic agent, comprising the steps of: dissolving said material in a first liquid component of an emulsion system to form a solution; adding to the solution a second component of an emulsion system and an emulsifier to form a mixture and applying force to the mixture to transform the mixture into an emulsion comprising a continuous phase and a dispersed phase in which the dispersed phase comprises globules of the material dissolved in the first liquid component, said globules having a diameter of between 10 and 200 nm; and treating the emulsion with an additional amount of a liquid miscible with the first and second components, thereby transforming the emulsion into a liquid-solid suspension comprising nanoparticles of the material. This is obvious variation in view of claims 1-20 of the patent which disclose a method for making nanopadicles of a substantially water insoluble material such as a hormone, an anti-inflammatory agent, or an anticancer agent, comprising the same method steps. Since both the claims of instant application and the claims of the patent are directed to a method for making nanoparticles of a substantially water insoluble material such as an anticancer agent by forming an emulsion system, in which a solution of the material forms the globules of a dispersed phase, and the emulsions are readily transformed into a single uniform liquid phase in which nanoparticles of compounds are suspended upon dilution with the external or continuous phase. Thus, claims 26-28 in present application and claims 20 in the patent are obvious variations of a method for making nanopadicles of a substantially water insoluble material such as an anticancer agent.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 26-28 and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of making nanoparticles of a substantially water insoluble material of a hormone, anticancer agent or anti-inflammatory agent such as progesterone, testosterone, methotrexate or ibuprofen, comprising the steps of: dissolving the material in a first liquid component of an emulsion system to form a solution; adding to the solution a second component of an emulsion system and an emulsifier to form a mixture and applying force to the mixture to transform the mixture into an emulsion comprising a continuous phase and a dispersed phase in which the dispersed phase comprises globules of the material dissolved in the first liquid component, said globules having a diameter of between 10 and 200 nm; and treating the emulsion with an additional amount of a liquid miscible with the first and second components, thereby transforming the emulsion into a liquid-solid suspension comprising the nanoparticles of the material, does not reasonably provide enablement for a method of making nanoparticles of a substantially water insoluble material of an antimicrobial agent, an antibacterial agent, an antifungal agent, an antiviral agent, an anti-HIV drug, an immunosuppressant, an anticancer agent or an antidiabetic agent, where the structure of the substantially water insoluble material or the emulsion system is not defined. The specification does not enable persons skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 26-28 and 33 encompass a method of making nanoparticles of a substantially insoluble water material of an antimicrobial agent, an antibacterial agent, an antifungal agent, an antiviral agent, an anti-HIV drug, an immunosuppressant, an anticancer agent or an antidiabetic agent. The specification, however, only discloses cursory conclusions (sees page 4-5), without data to support the findings, which state that the instant invention provides a method of making nanoparticles of a substantially water insoluble pharmaceutical compound from an emulsion system, in which a solution of the compound forms the globules of a dispersed phase, and the emulsions are readily transformed into a single uniform liquid phase in which nanoparticles of compounds are suspended upon dilution with the external or continuous phase. There are no indicia that the present application enables the full scope in view of a method of making nanoparticles of a water insoluble pharmaceutical compound as discussed in the stated rejection. The present application provides does not provide sufficient teaching/guidance as to how the full scope of the claims is encompassed. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the substantially water insoluble material of an antimicrobial agent, an antibacterial agent, an antifungal agent, an antiviral agent, an anti-HIV drug, an immunosuppressant, an anticancer

agent or an antidiabetic agent, and the emulsion system, where are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

Examples 1-4 indicates the making of nanoparticles of progesterone, testosterone, methotrexate and ibuprofen using triethyl citrate-water as the emulsion system. There are no working examples indicating the claimed methods in association with variants of a therapeutic agent and an emulsion system.

(3). The state of the prior art and relative skill of those in the art:

The specification indicates there are two major techniques, wet grinding and antisolvent technique, to produce solid drug nanoparticles (pages 2-3). However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the identification of substantially water insoluble agents from numerous antimicrobial agents, antibacterial agents, antifungal agents, antiviral agents, anti-HIV drugs, immunosuppressants, anticancer agents and antidiabetic agents, and the emulsion system used to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The specification describes substantially water insoluble materials as materials that have water solubility of less than 0.1%, however, the specification has not identified substantially a water insoluble material from numerous antimicrobial agents, antibacterial agents, antifungal agents, antiviral agents, anti-HIV drugs, immunosuppressants, anticancer agents and antidiabetic, nor has demonstrated the use of a particular emulsion system for the preparation of nanoparticles

of these agents. The invention is highly unpredictable regarding what therapeutic agents can be made as nanoparticles and what emulsion system can be used in the claimed method.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method of making nanoparticles of a substantially insoluble water material of an antimicrobial agent, an antibacterial agent, an antifungal agent, an antiviral agent, an anti-HIV drug, an immunosuppressant, an anticancer agent or an antidiabetic agent. However, the specification only demonstrates nanoparticles of certain water insoluble therapeutic agents (e.g., progesterone, testosterone, methotrexate and ibuprofen) are made using a specific emulsion system such as triethylcitrate-water (Examples 1-4), there is no indication making nanoparticles of various substantially water insoluble agents with various emulsion systems. The specification has not identified or demonstrated the making of nanoparticles of water insoluble materials of an antimicrobial agent, an antibacterial agent, an antifungal agent, an antiviral agent, an anti-HIV drug, an immunosuppressant, an anticancer agent or an antidiabetic agent with diverse structures and differing molecular weight using various emulsion systems. Moreover, there are no working examples indicating the making of nanoparticles of these substantially insoluble water agents using various emulsion systems. Since the specification does not provide specific guidance on the identification of substantially water insoluble materials among numerous of therapeutic agents, and various emulsion systems, it is necessary to have additional guidance and to carry out further experimentation to identify the substantially water insoluble materials and the emulsion system for preparing nanoparticles of a substantially water insoluble agent.

(6). Nature of the Invention

The scope of the claims includes making nanoparticles of substantially water insoluble materials of numerous therapeutic agents using an emulsion system, but the specification does not provide sufficient teachings on the identification of a substantially water insoluble material from numerous therapeutic agents and on the selection of an emulsion system used in the claimed method. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed methods associated with variants, and the guidance/the teaching in the specification is limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the emulsion system used for making nanoparticles of various therapeutic agents.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 27 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 27 and 28 are indefinite as to the emulsion system comprises an alcohol having two to ten carbon atoms and a concentration in water of about 5% to about 95%, it is not clear what role the alcohol plays in the emulsion system, e.g., whether alcohol is a first liquid component or a second liquid component, or along with water as a second liquid component. Note an alcohol such as ethanol is miscible with water. Claim 28 is included in the rejection

because it is dependent on a rejected claim and does not correct the deficiency of the claim from which it depends.

Conclusion

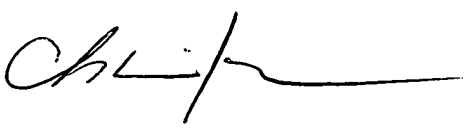
6. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner



CHIH-MIN KAM
PATENT EXAMINER

CMK
June 6, 2005